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Reaction Constants Derived from Activation Parameters for the Evaluation of Substituent and Solvent Effects

Ferenc Ruff

Department of Organic Chemistry, L. Eötvös University P. O. Box 32, H–1518 Budapest 112,
Hungary

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Reaction Constants Derived from Activation Parameters for the Evaluation of Substituent and Solvent Effects[#]

Ferenc Ruff*

Department of Organic Chemistry, L. Eötvös University P. O. Box 32, H-1518 Budapest 112, Hungary

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Abstract

In order to separate the effect of substituents into two parts, referring to the interaction of the reacting molecules and the solvation, the $\delta\Delta G^\ddagger$, $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ reaction constants were defined and determined from the dependence of ΔG^\ddagger , ΔH^\ddagger and ΔS^\ddagger activation parameters on the σ substituent constants, by analogy with the Hammett equation. The new reaction constants give the effect of the substituents on the reaction in energy units. $\delta\Delta G^\ddagger$, $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ can be divided into internal ($\delta\Delta X_{\text{int}}^\ddagger$, $X = G, H, S$) and external ($\delta\Delta X_{\text{ext}}^\ddagger$) parts which refer to the bond formation and the solvation, respectively. The contribution of the substituents to the internal part of entropy of activation ($\delta\Delta S_{\text{int}}^\ddagger$), and the external part of free energy of activation ($\delta\Delta G_{\text{ext}}^\ddagger$), originated from solvent reorganization were supposed to be zero. Thus $\delta\Delta G^\ddagger$ and $\delta\Delta S^\ddagger$ present a good approximation to $\delta\Delta H_{\text{int}}^\ddagger$ and $\delta\Delta S_{\text{ext}}^\ddagger$, describing the effect of substituents on the energy barrier of the reaction and on the solvation, respectively. The $\delta\Delta G^\ddagger$ reaction constant is interpreted in the same way as the ρ constant in the Hammett equation. The $\delta\Delta S^\ddagger$ reaction constant reflects the change in solvation with the substituents in the reaction. A tentative interpretation of $\delta\Delta S^\ddagger$, based on the solvation of charged species in organic solvents and the rearrangement of the solvent structure in water containing mixtures is discussed for some nucleophilic addition, nucleophilic substitution and acid-catalyzed reactions. A break of the $\delta\Delta H^\ddagger$ vs. σ and $\delta\Delta S^\ddagger$ vs. σ plots at about $\sigma \sim 0$ is diagnostic for the change of solvation with the electronic effect of the substituents. The $\delta\Delta S^\ddagger$ reaction constants can be used to describe change of solvation with the substituents for a reaction in a solvent.

Keywords. Substituent effect; solvent effect; activation parameters; reaction constants; QSPR; isokinetic relationships.

Abbreviations and notations

β , isokinetic temperature	$\delta\Delta S^\ddagger$, entropy of activation reaction constant
$\delta\Delta G^\ddagger$, free energy of activation reaction constant	$\delta\Delta X_{\text{int}}^\ddagger$, internal reaction constant
$\delta\Delta H^\ddagger$, enthalpy of activation reaction constant	$\delta\Delta X_{\text{ext}}^\ddagger$, external reaction constant

1 INTRODUCTION

In previous papers [1,2] the reaction constants $\delta\Delta G^\ddagger$, $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ were defined by Eqs. (1)–(3) indicating the dependence of the activation parameters on substituent constants, by the analogy with the Hammett equation, Eq. (4), [3–6].

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* Correspondence author; phone: +36–1–2090–555; fax: +36–1–3722–620; E-mail: ruff@szerves.chem.elte.hu.

$$\Delta G^\ddagger = \delta\Delta G^\ddagger\sigma + \Delta G_0^\ddagger \quad (1)$$

$$\Delta H^\ddagger = \delta\Delta H^\ddagger\sigma + \Delta H_0^\ddagger \quad (2)$$

$$\Delta S^\ddagger = \delta\Delta S^\ddagger\sigma + \Delta S_0^\ddagger \quad (3)$$

$$\log k = \rho\sigma + \log k_0 \quad (4)$$

ΔG^\ddagger , ΔH^\ddagger , ΔS^\ddagger and ΔG_0^\ddagger , ΔH_0^\ddagger , ΔS_0^\ddagger are the activation parameters obtained for the substituted and unsubstituted compounds, respectively. In Eqs. (1)–(3) σ substituent constants giving the best correlations with the Hammett equation were used. The Hammett ρ and σ constants are non-dimensional. The units of $\delta\Delta G^\ddagger$ and $\delta\Delta H^\ddagger$ reaction constants are $\text{kJ mol}^{-1} \sigma^{-1}$ and that of $\delta\Delta S^\ddagger$ is $\text{J mol}^{-1} \text{K}^{-1} \sigma^{-1}$, but σ can be replaced by any other substituent constant. The relation between the new reaction constants is the same as that of the activation parameters, Eq. (5).

$$\delta\Delta G^\ddagger = \delta\Delta H^\ddagger - T \delta\Delta S^\ddagger \quad (5)$$

The ratio of $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ reaction constants is equal to the β isokinetic temperature (Eq. 6, [1]), which is the slope of the linear ΔH^\ddagger vs. ΔS^\ddagger plots (Eq. 7) and the temperature of intersection of the $\log(k/T)$ vs. $(1/T)$ plots of a reaction series [7–11].

$$\delta\Delta H^\ddagger / \delta\Delta S^\ddagger = \beta \quad (6)$$

$$\Delta H^\ddagger = \beta\Delta S^\ddagger + \text{const.} \quad (7)$$

The new reaction constants can be determined by Eqs. (1)–(3) or from the β isokinetic temperature, as described earlier [1]. The reaction constants $\delta\Delta G^\ddagger$ and ρ have opposite signs and are proportional to each other, Eq. (8). $\delta\Delta G^\ddagger$ and ρ are calculated at the T temperature.

$$\delta\Delta G^\ddagger = -2.303RT\rho \quad (8)$$

If $\delta\Delta G^\ddagger$, $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ are positive, the electron-withdrawing substituents ($\sigma > 0$) increase and the electron-donating groups ($\sigma < 0$) decrease the value of the corresponding activation parameters, Eqs. (1)–(3), and vice versa for the case when these reaction constants have a negative sign. The decrease of ΔG^\ddagger and ΔH^\ddagger and the increase of ΔS^\ddagger accelerate the reaction.

On the basis of the theory developed by Heppler [12–14] the reaction constants can be divided into internal and external parts [1], referring to the bond formation and the solvation process, respectively, Eqs. (9)–(11).

$$\delta\Delta G^\ddagger = \delta\Delta G_{\text{int}}^\ddagger + \delta\Delta G_{\text{ext}}^\ddagger \quad (9)$$

$$\delta\Delta H^\ddagger = \delta\Delta H_{\text{int}}^\ddagger + \delta\Delta H_{\text{ext}}^\ddagger \quad (10)$$

$$\delta\Delta S^\ddagger = \delta\Delta S_{\text{int}}^\ddagger + \delta\Delta S_{\text{ext}}^\ddagger \quad (11)$$

The internal part of entropy of activation was supposed to be independent of the substituents [8,12–14] (*i.e.* $\delta\Delta S_{\text{int}}^\ddagger \approx 0$), and the external part of free energy of activation, due to solvent reorganization, to be zero ($\delta\Delta G_{\text{ext}}^\ddagger \approx 0$) [15–17]. If these approximations are valid, then $\delta\Delta S^\ddagger \approx \delta\Delta S_{\text{ext}}^\ddagger$, $\delta\Delta H_{\text{ext}}^\ddagger \approx T\delta\Delta S_{\text{ext}}^\ddagger$ and $\delta\Delta G^\ddagger \approx \delta\Delta H_{\text{int}}^\ddagger$. This means that the change of entropy with the

substituents is determined by the solvation. The value of $\delta\Delta H^\ddagger$ is also influenced by the solvation and the change of free energy of activation by the substituents is a good approximation of the internal part of enthalpy of activation, which is characteristic of the effects of substituents on the reaction.

Earlier it was supposed [1] that $\delta\Delta H_{\text{int}}^\ddagger$ does not change with a small change of the composition of the solvent and the so-called isosolvent temperature (β_{ext}), which can be obtained from a $\Delta H^\ddagger = \beta_{\text{ext}}\Delta S^\ddagger + \text{const.}$ plot of a reaction measured in different solvents, describes better the proportionality of $\delta\Delta H_{\text{ext}}^\ddagger$ and $\delta\Delta S_{\text{ext}}^\ddagger$. However, a more thorough analysis of the solvent effect [2] revealed that the latter approximation ($\delta\Delta H_{\text{ext}}^\ddagger/\delta\Delta S_{\text{ext}}^\ddagger \approx \beta_{\text{ext}}$) is valid only in a few special cases and the former approximation ($\delta\Delta H_{\text{ext}}^\ddagger/\delta\Delta S_{\text{ext}}^\ddagger \approx T$) gives regularly a much better description of the phenomena.

On the basis of the previous discussion the most valuable information can be expected from $\delta\Delta G^\ddagger$ and $\delta\Delta S^\ddagger$ reaction constants, which characterize the effects of substituents on the energy barrier of activation and on the difference of solvation between the reactants and the transition state, respectively. The interpretation of the $\delta\Delta H^\ddagger$ parameter is less straightforward, because it contains contributions not only from the internal but also from the external part of the enthalpy of activation, which is related to the entropy of activation and for a reaction may show considerable changes with the solvent. In this paper some simple organic reactions are discussed to find the first approximate correlations between the reaction constants and the mechanism of the reactions as well as the solvation of the participating species.

2 MATERIALS AND METHODS

Activation parameters were calculated from the temperature dependence of rate constants, by using the Eyring equation, Eq. (12):

$$\log(k/T) = \log(R/Nh) + \Delta S^\ddagger/2.303R - \Delta H^\ddagger/2.303RT = \log(R/Nh) - \Delta G^\ddagger/2.303RT \quad (12)$$

Because the temperature dependence of the activation parameters [18,19] all compounds of a reaction series should be measured in the same temperature range. ΔH^\ddagger and ΔS^\ddagger values calculated by Eq. (12) correspond to the mean temperature of the experimental range. Regularly only two activation parameters, ΔG^\ddagger and ΔH^\ddagger (seldom ΔG^\ddagger and ΔS^\ddagger) give good correlations ($r > 0.950$) with the substituent constants (Eqs.(1)–(3), [1]). Standard errors of the $\delta\Delta G^\ddagger$, $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ reaction constants are at about $\pm 5\%$, $\pm 10\%$ and $\pm 20\%$, respectively, but the value of the latter two can be even $\pm 40\%$ if the absolute values the $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ reaction constants are small. In these cases a more accurate value of $\delta\Delta S^\ddagger$ or $\delta\Delta H^\ddagger$ can be calculated from Eq. (5). Tables 1–4 contain the calculated $\delta\Delta G^\ddagger$, $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ as well as the measured ΔG_o^\ddagger , ΔH_o^\ddagger , ΔS_o^\ddagger values, the number of the investigated compounds (N) and the correlation coefficient (r) for preliminary information. Detailed statistical data (standard errors, F–statistic, standard deviation of the fit, calculated ΔG_o^\ddagger , ΔH_o^\ddagger , ΔS_o^\ddagger

values, leave-one out prediction, calculated by Origin 6.1 program) are given in Tables 5–8 in supplementary material. Only those compounds (given in Tables 1–4) were omitted from the calculations, which caused a change in the mechanism of the reaction, or whose activation parameters showed a decided difference from the expected values, presumably because of experimental errors. In the studied reaction series only a substituent of one of the reactants was varied. In some cases the changes of activation parameters with the substituents are also illustrated in $\Delta G^\ddagger/\Delta H^\ddagger/-T\Delta S^\ddagger$ vs. σ plots. For the evaluation of the $\delta\Delta G^\ddagger$, $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ reaction constants, the rate constants published earlier were used. References are given in Tables.

3 RESULTS AND DISCUSSION

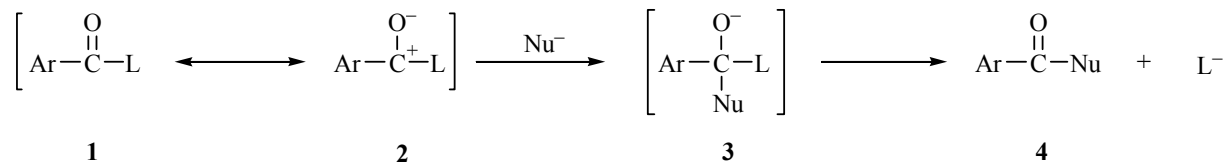
The interpretation of the reaction constant $\delta\Delta G^\ddagger$ is analogous to that of the well known ρ constant, which is widely used [3–6] since Hammett published his famous equation, Eq. (4). The advantage of $\delta\Delta G^\ddagger$ is revealed in giving the change of reactivity in energy units. We will also discuss the reaction constants $\delta\Delta S^\ddagger$ which shows the dependence of solvation on substituents.

Solvation is a highly complicated process which depends on structure of the reactants, the mechanism of the reaction and the solvent [20]. Each of the reactions may represent a special case, therefore only some general principles may be discussed here. During the reaction the reactants are desolvated, the transition state is solvated and some part of the solvent is reorganized. The desolvation of the reactants increases, the solvation of the transition state decreases the entropy of activation. Charged and dipolar species require stronger solvation than nonpolar molecules. The entropy change connected with the rearrangement of the solvent depends on its structure. In less polar solvents, the solvation of charged species give rise to stronger rearrangement of the solvent and a greater decrease of entropy of activation because the solvent molecules are only slightly ordered in the pure solvents. In polar protic solvents, especially in water, where the solvent molecules are highly ordered, the ordering can be smaller in the solvation shell of large ions or polar molecules, than in the pure solvent. In this way, given substituents in the reactant may either increase or decrease the entropy of activation, depending on the solvent.

3.1 Reaction of Carboxylic Acids Derivatives with Nucleophiles

The structure of aromatic carbonyl compounds can be characterized by two Lewis structures (**1**, **2**). The attack of the nucleophile on the carbonyl carbon atom leads to a tetrahedral intermediate (**3**) and the product (**4**) is formed with the splitting of the L leaving group [21]. From the Hammond principle [22] it follows that the structure of the transition state may be similar to that of the intermediate **3**. Electron-withdrawing and electron-donating substituents increase the contribution of Lewis structures **1** and **2**, respectively, and compounds with the latter substituents may bring about a greater negative charge on the carbonyl oxygen atom than the former ones. In the transition

state, with a nearly complete negative charge on the oxygen, the substituents have smaller effect on the charge distribution because only inductive effects are operative for the lack of delocalization. Thus the differences in the charges of the carbonyl oxygen atom of the different substituted compounds are greater in the reactant state than in the transition state.



In reactions solvation can be changed in different ways; some cases are discussed below.

1. If the solvation is influenced mainly by the size of the charge of the substrate in less polar solvents, then the decrease of entropy at the formation of the transition state is smaller, ΔS^\ddagger is greater for compounds with electron-donating groups ($\sigma < 0$); *i.e.* $\delta\Delta S^\ddagger < 0$, *cf.* Eq. (3). Compounds with electron-donating groups are solvated stronger in the reactant state than those having electron-withdrawing substituents and they can be transferred to the transition state with a smaller change in the rearrangement of the solvent molecules.

2. If the nucleophile is strongly solvated in a polar protic solvent and its attack on less reactive compounds with electron-donating groups must be promoted by a special solvation of the carbonyl oxygen in the transition state, then entropy of activation shows a greater decrease, ΔS^\ddagger is smaller for the given compounds ($\sigma < 0$) than in other cases; *i.e.* $\delta\Delta S^\ddagger > 0$, *cf.* Eq. (3). In polar protic solvents (*e.g.* in water) the solvent molecules in the solvation shell of large ions are less ordered than in the bulk of the solvent. Because the electron-withdrawing groups decrease the negative charge of the oxygen atom in the transition state, this phenomenon can also lead to a less ordered solvent shell and to an increase in ΔS^\ddagger for these reactants ($\sigma > 0$); *i.e.* $\delta\Delta S^\ddagger > 0$, *cf.* Eq. (3).

3. If the splitting of the leaving group (L) is rate-determining and promoted by solvation, electron-withdrawing substituents in the aromatic ring (Ar) linked directly to the C=O group hinder the departing of L^- . These compounds ($\sigma > 0$) need stronger solvation which is connected with the decrease in ΔS^\ddagger value; *i.e.* $\delta\Delta S^\ddagger < 0$. On the other hand, electron-withdrawing groups in the L leaving group promote the reaction and need smaller solvation, therefore ΔS^\ddagger increases; *i.e.* $\delta\Delta S^\ddagger > 0$.

In the alkaline hydrolysis ($\text{Nu} = \text{OH}^-$) of ArCOOEt substrates [23–28], the values of $\delta\Delta G^\ddagger$ reaction constants are similar in different solvents (Table 1, Nos. 1a–1f). $\delta\Delta G^\ddagger < 0$ was found because electron-withdrawing groups decrease the value of ΔG^\ddagger and increase the rate of the reaction. The values of $\delta\Delta H^\ddagger$ are not characteristic of the reaction, but depend clearly on the solvent. In aqueous solvent mixtures $\delta\Delta S^\ddagger > 0$, if the concentration of water is higher than about 20 %, and it increases with the increase of the water content of the solvent.

Table 1. Reaction constants and activation parameters for the reactions of carboxylic acid derivatives with nucleophiles

No	Reaction	Ref.	Solvent ^a	N ^b	$\delta\Delta G^\ddagger_{c,d}$ (r)	$\delta\Delta H^\ddagger_{c,d}$ (r)	$\delta\Delta S^\ddagger_{c,e}$	$\Delta G^\ddagger_{c,f}$	$\Delta H^\ddagger_{c,f}$	$\Delta S^\ddagger_{c,g}$
1a.	ArCOOEt + OH ^{-h}	[23–25]	56 wt % a–w ^k	18	–13.2 (0.991)	–11.2 (0.984)	6.7	87.5	58.2	–98.3
1b.		[25]	50 vol % a–w	5	–12.3 (0.996)	–7.98 (0.946)	14.5	87.1	55.4	–106
1c.		[25]	40 vol % a–w	6	–12.7 (0.998)	–6.58 (0.969)	20.5	86.4	52.6	–113
1d.		[26]	71.2 wt % m–w	6 ^l	–12.5 (0.998)	–6.19 (0.975)	21.2	91.5	71.8	–66.1
1e.		[27]	85 wt % e–w	8	–14.7 (0.997)	–15.8 (0.998)	–3.7	93.3	71.5	–67.4
1f.		[28]	85 wt % e–w	6	–14.5 (0.996)	–14.4 (0.991)	~0	91.3	71.5	–66.5
2.	MeCOOAr ^r + OH ⁻ⁱ	[23]	56 wt % a–w	5 ^m	–8.44 ⁿ (1.000)	–8.35 (0.999)	~0	73.8 ⁿ	51.0	–78.8
3a.	PhCOOAr ^r + OH ⁻ⁱ	[30,31]	w	7	–6.07 (0.993)	–5.19 (0.981)	2.95	75.2	42.5	–110
3b.		[32]	80 vol % dm–w	6 ^o	–9.44 (0.998)	–16.0 (0.991)	–22.0	69.7	36.5	–111
3c.		[33]	2.25 M Bu ₄ NBr (w)	6 ^o	–13.0 (0.997)	–24.9 (0.976)	–39.6	79.3	63.3	–53.3
4.	ArCONH ₂ + OH ^{-h}	[34]	60 vol % e–w	4	–8.49 ^p (1.000)	–12.6 (0.991)	–12.6	111.7 ^p	75.2	–112
5.	(ArCO) ₂ O + H ₂ O ^h	[35]	75 vol % d–w	9	–19.8 ^q (0.994)	–31.3 (0.971)	–38.6	102.7 ^q	64.1	–151
6.	ArCOCl + H ₂ O ^h	[36]	95 vol % a–w	4 ^r	–11.2 (1.000)	–23.0 (0.998)	–39.6	97.4	49.0	–163
7a.	ArCOCl + EtOH ^h	[37]	e	6 ^r	–8.83 (0.988)	–15.4 (0.989)	–22.0	90.9	61.5	–98.7
7b.		[38]	60 vol % eth–e	6 ^r	–10.4 (0.989)	–16.6 (0.988)	–20.8	95.7	57.9	–127
8.	ArCOCl + PhNH ₂ ^h	[39]	b	4	–6.85 (0.993)	–9.34 (0.994)	–8.36	79.5	28.9	–170
9a.	ArNH ₂ + PhCOCl ^j	[39]	b	5	14.2 (0.992)	14.0 (0.975)	~0	79.9	30.7	–165
9b.		[40]	eth	4	14.8 (0.993)	19.3 (0.999)	15.1	77.5	22.9	–183

^a Solvents: (a) acetone, (b) benzene, (d) dioxane, (dm) DMSO, (e) ethanol, (eth) ether, (m) methanol, (w) water. Values of solvent composition refer to the first solvent.

^b Number of compounds.

^c The values of $\delta\Delta G^\ddagger$ and $\Delta G^\ddagger_{c,f}$ were calculated at 298 K, if not otherwise stated.

^d In kJ mol⁻¹σ⁻¹ unit.

^e In J mol⁻¹ K⁻¹ σ⁻¹ unit. Values given without correlation coefficient are calculated from Eq. (5).

^f In kJ mol⁻¹ unit.

^g In J mol⁻¹ K⁻¹ unit.

^h σ constants were used in correlations.

ⁱ σ^o constants were used in correlations.

^j σ^r constants were used in correlations.

^k 56 wt % a–w and 60 vol % a–w are identical.

^l *p*-Cl substituted compound omitted.

^m *p*-NH₂, *m*-COO⁻ and *p*-COO⁻ substituted compounds omitted.

ⁿ The value of $\delta\Delta G^\ddagger$ and $\Delta G^\ddagger_{c,f}$ was calculated at 288 K.

^o *m*-NH₂ substituted compound omitted.

^p The values of $\delta\Delta G^\ddagger$ and $\Delta G^\ddagger_{c,f}$ were calculated at 326 K.

^q The values of $\delta\Delta G^\ddagger$ and $\Delta G^\ddagger_{c,f}$ were calculated at 331 K. ^r *p*-MeO substituted compound omitted.

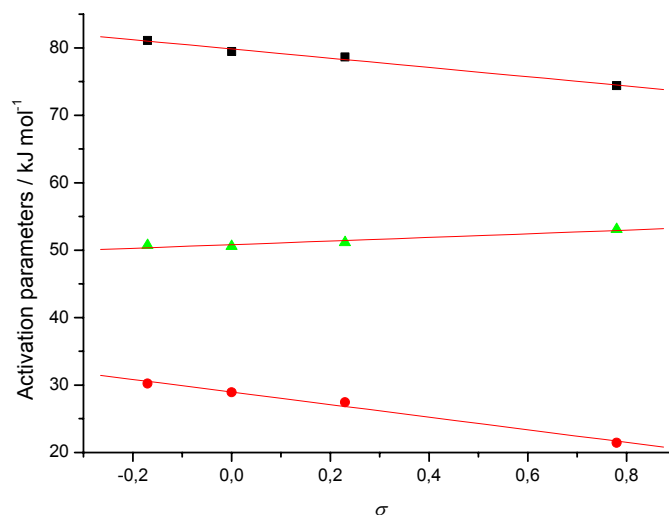


Figure 1. ΔG^\ddagger vs. σ (■—■), ΔH^\ddagger vs. σ (●—●), and $-T\Delta S^\ddagger$ vs. σ (▲—▲) plots of the reaction of aniline (PhNH_2) with substituted benzoyl chlorides ($\text{X}-\text{C}_6\text{H}_4\text{COCl}$, $\text{X} = p\text{-Me, H, } p\text{-Cl, } p\text{-NO}_2$) in benzene, (Table 1. No. 8; [39]). Slopes: $\delta\Delta G^\ddagger = -6.85 \pm 0.6 \text{ kJ mol}^{-1} \sigma^{-1}$ ($r = 0.993$), $\delta\Delta H^\ddagger = -9.34 \pm 0.74 \text{ kJ mol}^{-1} \sigma^{-1}$ ($r = 0.994$), $-T\delta\Delta S^\ddagger = 2.70 \pm 0.56 \text{ kJ mol}^{-1} \sigma^{-1}$ ($r = 0.960$), $\delta\Delta S^\ddagger = -9.02 \pm 1.9 \text{ J mol}^{-1} \text{ K}^{-1} \sigma^{-1}$, $\delta\Delta S_{\text{calc}}^\ddagger = -8.36 \text{ J mol}^{-1} \text{ K}^{-1} \sigma^{-1}$ ($T = 298 \text{ K}$).

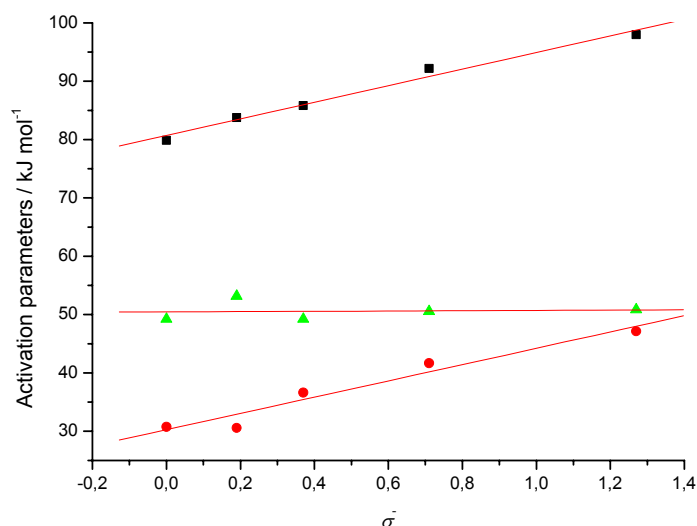


Figure 2. ΔG^\ddagger vs. σ^- (■—■), ΔH^\ddagger vs. σ^- (●—●), and $-T\Delta S^\ddagger$ vs. σ^- (▲—▲) plots of the reaction of substituted anilines ($\text{X}-\text{C}_6\text{H}_4\text{NH}_2$, $\text{X} = \text{H, } p\text{-Cl, } m\text{-Cl, } m\text{-NO}_2, p\text{-NO}_2$) with benzoyl chloride (PhCOCl) in benzene, (Table 1. No. 9a; [39]). Slopes: $\delta\Delta G^\ddagger = 14.2 \pm 1.1 \text{ kJ mol}^{-1} (\sigma^-)^{-1}$ ($r = 0.992$), $\delta\Delta H^\ddagger = 14.0 \pm 1.9 \text{ kJ mol}^{-1} (\sigma^-)^{-1}$ ($r = 0.975$), $-T\delta\Delta S^\ddagger = \sim 0 \text{ kJ mol}^{-1} (\sigma^-)^{-1}$, $\delta\Delta S^\ddagger = \sim 0 \text{ J mol}^{-1} \text{ K}^{-1} \sigma^{-1}$, ($T = 298 \text{ K}$).

In 85 wt % ethanol–water $\delta\Delta S^\ddagger \sim 0$, the change of solvation in this medium seems to be independent of the substituents. The increasing leaving group ability increases the value of entropy reaction constant. $\delta\Delta S^\ddagger = 27,0 \text{ J mol}^{-1} \text{ K}^{-1} \sigma^{-1}$ was obtained for the hydrolysis of $\text{ArCOOAr}'$ benzoic acid esters with the $\text{Ar}'\text{O} = 2,4\text{-(NO}_2)_2\text{-C}_6\text{H}_3\text{O}$ leaving group in 50 vol % dioxane–water mixture ($\delta\Delta G^\ddagger = -13.5 \text{ kJ mol}^{-1} \sigma^{-1}$, $\delta\Delta H^\ddagger = -5.81 \text{ kJ mol}^{-1} \sigma^{-1}$, [29]). The change of solvation with the substituents may be explained by reasons discussed above as case 2 and 3. The ΔG_0^\ddagger value of the unsubstituted compound shows only smaller changes with the solvent composition (Table 1, Nos.1a–1f). ΔS_0^\ddagger is much higher in alcohol–water mixtures, the solvation is changed more slightly at the formation of the transition state in these media.

If substituents are bonded to the phenyl ring of the Ar'O leaving group in MeCOOAr' ([23], Table 1, No. 2), they have smaller effect (the absolute value of $\delta\Delta G^\ddagger$ decreases as compared to that of ArCOOEt) and do not change solvation as shown by $\delta\Delta S^\ddagger \approx 0$ in 56 wt % acetone–water mixtures. The change in the solvation of the transition state with the substituents is the same as that of the reactant state.

In the basic hydrolysis of PhCOOAr' esters ([30–33], Table 1, Nos. 3a–3c) $\delta\Delta G^\ddagger$ shows considerable change with the solvent. $\delta\Delta S^\ddagger$ has a small positive value in water and high negative values in 80 vol % DMSO–water mixtures or in 2.25 M aqueous Bu₄NBr solution of high ionic strength. The OH[−] ion is less solvated and most reactive in DMSO–water and most solvated and less reactive in 2.25 M Bu₄NBr solution (*cf.* ΔG_o^\ddagger values in Table 1, Nos. 3a–3c). The change of solvation is the smallest in the reaction at high ionic strength (*cf.* ΔS_o^\ddagger values). The observed change in entropy of activation with the substituents may be explained for water ($\delta\Delta S^\ddagger > 0$) and for the other two media ($\delta\Delta S^\ddagger < 0$) as described in case 2 and case 1, respectively.

In some other reactions of substituted carboxylic acid derivatives with nucleophiles ([34–40] Table 1, Nos. 4–8) $\delta\Delta G^\ddagger < 0$ and $\delta\Delta S^\ddagger < 0$ were found in less polar solvents or in solvent mixtures containing small amount of protic solvent, and solvation is controlled by charges (case 1). The effect of substituents of the substrate on the activation parameters *e.g.* in the reaction of ArCOCl with PhNH₂ in benzene (Table 1, No. 8) is shown in Figure 1. By varying the substituents of the nucleophile in the reaction of PhCOCl with ArNH₂, $\delta\Delta G^\ddagger > 0$ was obtained, indicating that electron–donating groups ($\sigma < 0$) promote the reaction ([39]; Table 1, No. 9a, Fig. 2). In benzene solvation does not change with the substituents ($\delta\Delta S^\ddagger \sim 0$). In ether, however, aniline derivatives substituted with electron–withdrawing groups ($\sigma > 0$) form stronger H–bonds than those with electron–donating substituents, and the desolvation of the nucleophiles in the reaction increases the value of ΔS^\ddagger , *i.e.* $\delta\Delta S^\ddagger > 0$; [40], Table 1, No. 9b, *cf.* Eq. (3).

3.2 Aliphatic Nucleophilic Substitutions

In S_N2 type solvolysis reactions of alkyl benzenesulfonate (ArSO₃R) the water or alcohol (R'OH) nucleophiles attack the α –carbon atom of the R alkyl group with the formation of alcohols (ROH) or ethers (ROR'), respectively [41–43]. Electron–withdrawing substituents ($\sigma > 0$) bonded to the ArSO₃[−] leaving group promote the nucleophilic attack ($\delta\Delta G^\ddagger < 0$) and, by decreasing the charge and the solvation of the ArSO₃[−] ion, increase the entropy of activation ($\delta\Delta S^\ddagger > 0$). The less polar the solvent is, the greater the values of $\delta\Delta S^\ddagger$ and ΔG_o^\ddagger , and the smaller those of $\delta\Delta G^\ddagger$ and ΔS_o^\ddagger (Table 2, Nos. 1–4).

When the substituents in the nucleophile were varied in the S_N2 reaction of MeI with dimethylaniline derivatives (ArNMe₂), electron–donating groups ($\sigma < 0$) were found to promote the reaction ($\delta\Delta G^\ddagger > 0$) and to decrease the entropy of activation ($\delta\Delta S^\ddagger > 0$), which may be ascribed to

the increased solvation of the transition state ([44]; Table 2, No. 5).

Table 2. Reaction constants and activation parameters of aliphatic nucleophilic substitution reactions

No	Reaction ^a	Ref.	Solvent ^b	N ^c	T/ K ^d	$\delta\Delta G^\ddagger$ ^e (r)	$\delta\Delta H^\ddagger$ ^e (r)	$\delta\Delta S^\ddagger$ ^f (r)	ΔG_o^\ddagger ^g	ΔH_o^\ddagger ^g	ΔS_o^\ddagger ^h
1.	ArSO ₃ Me + H ₂ O	[41]	w	6	323	-5.72 (0.974)	-1.53	12.9 (0.973)	102.3	86.1	-50.2
2.	ArSO ₃ Me + EtOH	[42]	e	5	343	-9.29 (0.999)	-2.16	22.8 (0.946)	111.8	84.2	-80.3
3a.	ArSO ₃ nPr + ROH	[43]	m	6	313	-7.75 (0.989)	-2.35	17.2 (0.975)	111.8	88.9	-73.3
3b.			e	6	313	-8.05 (0.984)	-0.50	24.2 (0.963)	113.3	86.7	-84.9
3c.			n-p	6	313	-8.33 (0.986)	0.3	27.7 (0.977)	113.7	84.7	-92.6
3d.			n-b	6	313	-8.39 (0.988)	-1.77	21.1 (0.955)	114.0	85.9	-89.6
3e.			i-p	6	313	-9.16 (0.987)	-1.00	26.1 (0.957)	115.6	75.1	-127.0
3f.			t-b	6	313	-9.77 (0.990)	-0.64	29.2 (0.990)	118.6	76.3	-135.2
4a.	ArSO ₂ CH ₂ CH=CH ₂ + ROH	[43]	m	8	303	-8.39 (0.999)	-7.53 (0.929)	2.84	100.6	86.9	-45.1
4b.			n-p	8	303	-8.95 (0.998)	-4.77 (0.796)	13.8 (0.783)	103.1	86.3	-55.6
4c.			n-b	8	303	-9.22 (0.998)	-2.47 (0.868)	22.3 (0.970)	103.5	86.9	-54.9
4d.			i-p	8	303	9.36 (0.998)	-1.05	27.4 (0.962)	104.8	82.6	-73.3
4e.			t-b	8	303	-10.4 (0.998)	-2.93	24.8 (0.964)	106.1	67.4	-127.7
5.	ArNMe ₂ + MeI	[44]	m	7	328	13.8 (0.994)	16.7 (0.974)	8.84	100.9	61.6	-120
6.	ArNHCOCH ₂ Cl + PhNMe ₂	[45]	o	10	461	-0.70 (0.977)	-36.1 (0.993)	-77.2 (0.992)	137.0	81.5	-131.5
7.	ArNHQ + H ₂ O (Q=CH ₂ C(NO ₂) ₂ Me) ⁱ	[46]	pH: 7.02 (w)	14	298	13.8 (0.988)	26.1 (0.989)	41.4 (0.982)	87.9	76.1	-38.5

^a The σ constants were used in correlations if not otherwise stated.

^b Solvents: (b) BuOH, (e) EtOH, (m) MeOH, (p) PrOH, (o) octanol, (w) water. Values of solvent composition refer to the first solvent.

^c Number of compounds.

^d The values of ΔG_o^\ddagger and $\delta\Delta G^\ddagger$ were calculated at the given temperatures.

^e In kJ mol⁻¹ σ^{-1} unit. Values given without correlation coefficient are calculated from Eq.(5).

^f In J mol⁻¹ K⁻¹ σ^{-1} unit. Values given without correlation coefficient are calculated from Eq.(5).

^g In kJ mol⁻¹ unit.

^h In J mol⁻¹ K⁻¹ unit.

ⁱ The σ^- constants were used in correlations.

The $\delta\Delta S^\ddagger$ value obtained may be reasoned in two ways. Dimethylaniline derivatives with electron-withdrawing groups are more polar ($X^{\delta-}-C_6H_4-NMe_2^{\delta+}$) in the reactant state than the unsubstituted analogue and need a smaller change in solvation to reach the transition state. In contrast the charge separation for dimethylaniline derivatives with electron-donating groups is greater in the transition state ($X^{\delta+}-C_6H_4-NMe_2^{\delta+}\cdots Me\cdots I^{\delta-}$) and needs greater solvation. Both effects give rise to a greater decrease of entropy values at the formation of the transition state and

produce both a smaller value of ΔS^\ddagger for ArNMe₂ compounds with electron-donating groups ($\sigma < 0$) in Ar and a positive $\delta\Delta S^\ddagger$ reaction constant.

In the S_N2 type nucleophilic displacement reaction [45] involving *N,N*-dimethylaniline (**5**) and *N*-chloroacetyl arylamines (**6**) electron-withdrawing substituents on the Ar aromatic ring of the substrate help the nucleophilic attack ($\delta\Delta G^\ddagger < 0$) and increase the solvation of the transition state ($\delta\Delta S^\ddagger < 0$; Table 2, No. 6, Fig. 3). The absolute value of $\delta\Delta G^\ddagger$ is small, because the substituents in Ar are far from the CH₂ center of the reaction and the temperature of the measurements ($T = 461$ K) is close to the isokinetic temperature ($\beta = 467$ K). Both ΔS^\ddagger and $\delta\Delta H^\ddagger$ values are changed on a much larger scale because of solvation. The reason may be similar to that mentioned Section 3.1. Compounds with electron-donating groups have higher negative charge on the carbonyl oxygen atom (cf. Lewis structure **2**) and are solvated more strongly, therefore the rearrangement of the solvent molecules is smaller, and the entropy of activation is greater for the given compounds. The opposite can be expected for compounds with electron-withdrawing substituents.

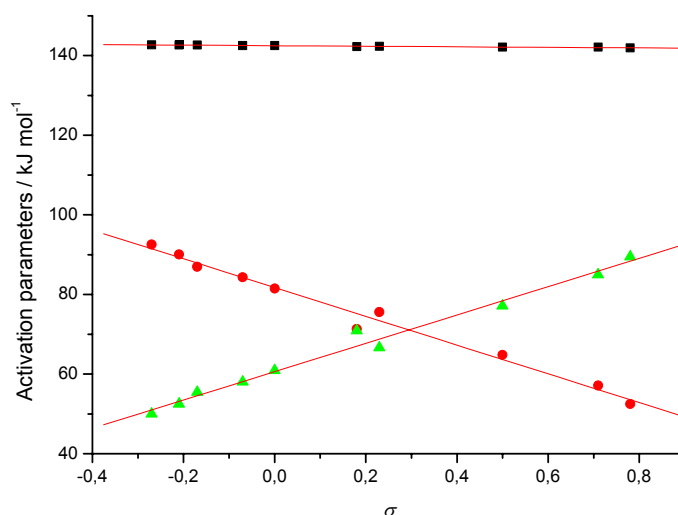
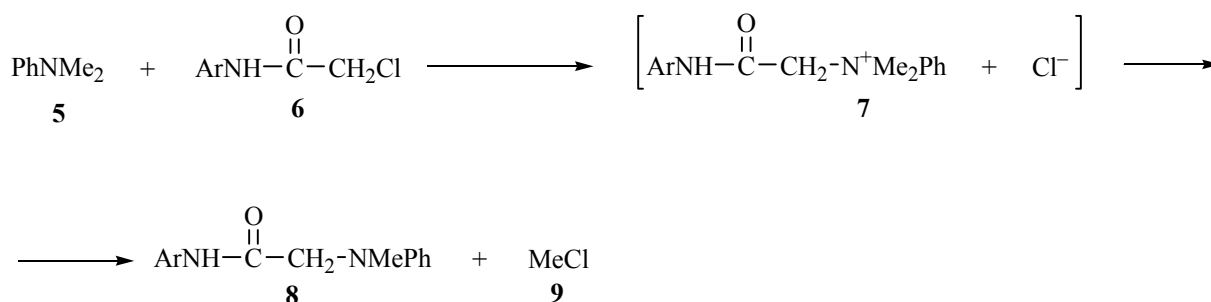
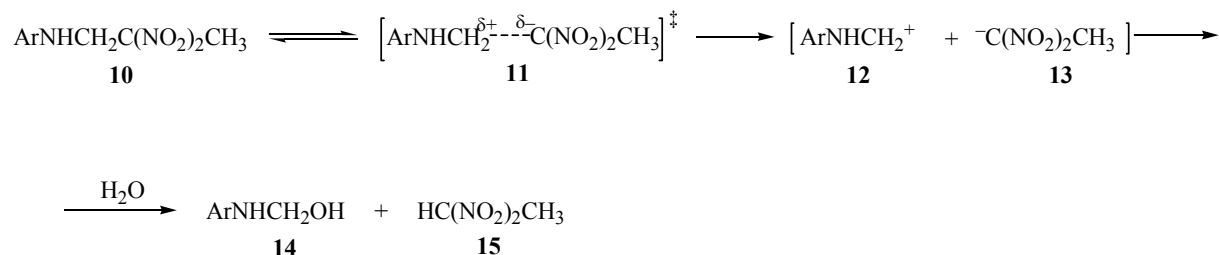


Figure 3. ΔG^\ddagger vs. σ (■–■), ΔH^\ddagger vs. σ (●–●), and $-T\Delta S^\ddagger$ vs. σ (▲–▲) plots of the reaction of substituted *N*-chloroacetyl arylamines ($\text{X}-\text{C}_6\text{H}_4\text{NHCOCH}_2\text{Cl}$, X = *p*-MeO, 3,4-Me₂, *p*-Me, *m*-Me, H, *p*-I, *p*-Br, *p*-CH₃CO, *m*-NO₂, *p*-NO₂) with *N,N*-dimethylaniline (PhNMe₂) in octanol, (Table 2, No. 6; [45]). Slopes: $\delta\Delta G^\ddagger = -0.7 \pm 0.05 \text{ kJ mol}^{-1} \sigma^{-1}$ ($r = 0.977$), $\delta\Delta H^\ddagger = -36.1 \pm 1.6 \text{ kJ mol}^{-1} \sigma^{-1}$ ($r = 0.993$), $-T\delta\Delta S^\ddagger = 35.6 \pm 1.6 \text{ kJ mol}^{-1} \sigma^{-1}$ ($r = 0.992$), $\delta\Delta S^\ddagger = -77.2 \pm 1.9 \text{ J mol}^{-1} \text{ K}^{-1} \sigma^{-1}$, ($T = 461$ K).

The *N*-(2,2-dinitropropyl) arylamines (**10**) hydrolyse [46] in an unimolecular S_N1 reaction in buffered neutral aqueous solution to give ionic intermediates (**12**, **13**), which react with water in a fast step to give the products (**14**, **15**). Electron-donating substituents accelerate the reaction ($\delta\Delta G^\ddagger > 0$, Table 2, No. 7), but activation parameters correlate with the σ^- constants because electron-withdrawing groups with through conjugation (*e.g.* *p*-NO₂) hinder the reaction in a greater degree than it would be expected on the basis of the σ constants.

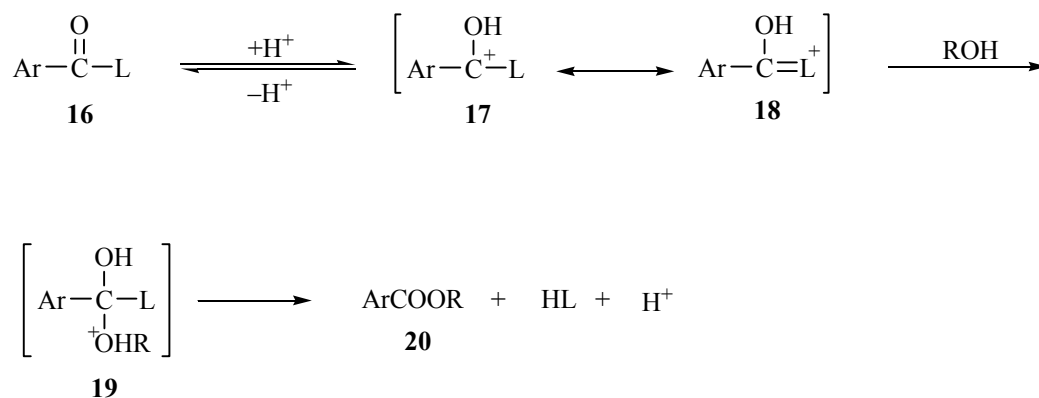


Electron-withdrawing groups increase the value of ΔS^\ddagger ($\delta\Delta S^\ddagger > 0$, Table 2, No. 7). The explanation may be the same as in the case of the S_N2 reaction of ArNMe₂ derivatives with MeI. As compared with the unsubstituted compounds the polarity of the reactants with electron-withdrawing substituents is greater in the reactants state, the change of their solvation is smaller at the formation of the transition state (**11**). When electron-donating substituents are present, the charge separation in the transition state is more extensive, requiring stronger solvation. Both effects produce a positive $\delta\Delta S^\ddagger$ value.

3.3 Acid-catalyzed Reactions

In acid-catalyzed reactions the first step is the equilibrium protonation of the substrate (**16–18**), which is followed by the nucleophilic attack in the second, rate-determining step (**19–20**). Activation parameters (ΔX^\ddagger , $X = G, H, S$), calculated from the observed rate constants are composed of the enthalpy and entropy changes (ΔX_1°) of the equilibrium and the activation parameters (ΔX_2^\ddagger) of the second step ($\Delta X^\ddagger = \Delta X_1^\circ + \Delta X_2^\ddagger$, [1]). If the protonation is a fast equilibrium, the change of free energy of activation with the substituents $\delta\Delta G^\ddagger$ has small absolute value, *e.g.* in the hydrolysis of esters [47–49] and amides [34,50] or in the esterification of carboxylic acids [51,52] (Table 3, No. 1–6).

In the hydrolysis of ArCOOEt esters the nucleophilic attack ($\delta\Delta G^\ddagger < 0$, Table 3, No. 1), in that of the MeCOOAr' and ArCONH₂ substrate the protonation has greater substituent effect ($\delta\Delta G^\ddagger > 0$, Table 3, Nos. 2,3), and they are promoted by electron-withdrawing and electron-donating groups, respectively. In the esterification of ArCOOH acids with methanol ([51]; Table 3, No. 5) the protonation, in the reaction of the same substrates with the bulky cyclohexanol ([52]; Table 3, No. 6) the nucleophilic attack has greater influence on the substituent effect.



L = OEt, OAr', NH₂; R = H, Me, C₆H₁₁

Table 3. Reaction constants and activation parameters of acid catalyzed reactions

No	Reaction ^a	Ref.	Solvent ^b	N ^c	T/ K ^d	$\delta\Delta G_o^{\ddagger e}$ (r)	$\delta\Delta H_o^{\ddagger e}$ (r)	$\delta\Delta S_o^{\ddagger f}$ (r)	$\Delta G_o^{\ddagger g}$	$\Delta H_o^{\ddagger g}$	$\Delta S_o^{\ddagger h}$
1a.	ArCOOEt + H ₃ O ⁺	[47]	56.74 wt % e-w	5	353	-1.54 (0.920)	-10.7 (0.992)	-26.0 (0.985)	118.7	81.5	-105
1b.		[47]	56 wt % a-w	8	353	-1.68 (0.808)	-3.34 (0.854)	-4.79 (0.724)	118.7	81.5	-105
2.	AcOAr + H ₃ O ⁺ ⁱ	[48, 49]	56 wt % a-w	5	298	0.94 (0.976)	-2.01 (0.951)	-9.89 (0.985)	99.2	69.1	-101
3.	ArCONH ₂ + H ₃ O ⁺	[34]	60 vol % e-w	4	326	2.69 (0.997)	11.3 (0.957)	26.3	115.4	93.8	-65.3
4a.	ArCONHN=CHPh + H ₃ O ⁺ ^j	[50]	pH: 1.15	6	298	-0.81 (0.999)	-40.4 (0.995)	-132.8 (0.994)	77.1	66.7	-34.8
4b.		[50]	pH: 4.01	6	298	0.94 (0.989)	-36.7 (0.998)	-125.8 (0.998)	89.2	36.5	-177
5.	ArCOOH + MeOH ₂ ⁺	[51]	MeOH	16	298	1.33 (0.464)	1.10 (0.228)	~ 0	94.3	61.7	-109
6.	ArCOOH + C ₆ H ₁₁ OH ₂ ⁺	[52]	C ₆ H ₁₁ OH	14	328	-3.46 (0.871)	-5.96 (0.407)	-7.83	110.7	79.0	-96.7
7.	ArCOOH + Ph ₂ CN ₂ ^k	[53]	toluene	8	298	-12.9 (0.999)	-9.03 (0.778)	13.0	84.1	54.4	-100
8.	PhCOOH + Ar ₂ CN ₂ ^k	[53]	toluene	8	298	9.59 (0.996)	5.16 (0.919)	-14.9	84.1	54.4	-100
9.	PhNH ₂ + ArNO ^l	[54]	94 vol % e-w acetate buffer ^m	5	329	-8.79 (0.984)	-21.2 (0.999)	-37.4 (0.996)	98.3	21.9	-232
10.	ArNH ₂ + PhNO ^l	[54]	94 vol % e-w acetate buffer ^m	4	329	16.2 (0.997)	20.0 (0.998)	12.1 (0.959)	98.3	21.9	-232

^a The σ constants were used in correlations if not otherwise stated

^b Solvents: (a) acetone, (e) EtOH, (w) water. Values of solvent composition refer to the first solvent

^c Number of compounds

^d The values of ΔG_o^{\ddagger} and $\delta\Delta G_o^{\ddagger}$ were calculated at the given temperatures

^e In kJ mol⁻¹ σ^{-1} unit. Values given without correlation coefficient are calculated from Eq. (5)

^f In J mol⁻¹ K⁻¹ σ^{-1} unit. Values given without correlation coefficient are calculated from Eq. (5)

^g In kJ mol⁻¹ unit

^h In J mol⁻¹ K⁻¹ unit

ⁱ The σ_o constants were used in correlations

^j Products: ArCONHNH₂ + PhCHO

^k Products: ArCOOCHPh₂ or PhCOOCHAR'₂

^l Product: PhN=NAr

^m 0.88 M AcOH + 0.25 M AcONa

The value of $\delta\Delta S^\ddagger$ (and therefore that of $\delta\Delta H^\ddagger$) depends on the effect of the substituents on solvation. In the hydrolysis of esters (Table 3, Nos. 1, 2) and N-acyl hydrazones (Table 3, No. 4) and in the esterification (Table 3, No. 6) the reactants substituted with an electron-donating group in Ar (*cf.* Lewis structure **17**) are solvated stronger, therefore the change of the solvation at the formation of the transition state is smaller for the given compounds ($\delta\Delta S^\ddagger < 0$). In the case of amides (Table 3, No. 3) for which $\delta\Delta S^\ddagger > 0$, compounds with electron-withdrawing substituents (*cf.* Lewis structure **18**) have more polar structure and are solvated in a greater extent in the reactant state and require therefore smaller reorganization in the solvation shell at the formation of the transition state. These compounds exhibit higher entropy of activation.

In the reaction of aromatic carboxylic acids (ArCOOH) with diaryldiazometanes (Ar'₂CN₂) [53] the proton transfer to the C-atom of Ar'₂CN₂ is the rate-determining step, which is promoted by the electron-withdrawing groups in ArCOOH ($\delta\Delta G^\ddagger < 0$) and by the electron-donating substituents in Ar'₂CN₂ ($\delta\Delta G^\ddagger > 0$, Table 3, Nos. 7, 8). The delocalisation of the charge in the ArCOO⁻ intermediate is aided by electron-withdrawing groups ($\delta\Delta S^\ddagger > 0$). If Ar'₂CN₂ is the reactant, the electron-donating groups have similar effect on the Ar'₂CHN₂⁺ intermediate ($\delta\Delta S^\ddagger < 0$), decreasing the solvation and increasing the value of ΔS^\ddagger .

In the reaction of arylamines (ArNH₂) with aromatic nitroso compounds (Ar'NO) [54] acid catalysis takes place mainly by H-bond formation with Ar'NO. The rate-determining step is the nucleophilic attack of the amino-nitrogen atom on the nitroso group (products are ArN=NAr' + H₂O). The reaction is facilitated by the electron-donating groups of ArNH₂ ($\delta\Delta G^\ddagger > 0$, Table 3, No. 10) and the electron-withdrawing groups of Ar'NO ($\delta\Delta G^\ddagger < 0$, Table 3, No. 9). The electron-donating groups in Ar'NO and the electron-withdrawing groups in ArNH₂ increase the charge separation and the solvation in the reactant state and this way increase the value of ΔS^\ddagger (*cf.* $\delta\Delta S^\ddagger$ values for reactions Nos. 9 and 10 in Table 3).

3.4 Reactions with Changing Solvation

In some reactions the ΔH^\ddagger vs. σ and ΔS^\ddagger vs. σ plots have two linear parts with a break at about $\sigma \approx 0$ (Figs. 4 and 5. Note that entropy is plotted in $-T\Delta S^\ddagger$ units, to have the plot on the same scale as ΔG^\ddagger and ΔH^\ddagger). The same type of plots were obtained in every known cases. Here Eqs. (1)–(3) should be applied separately for compounds having electron-donating or electron-withdrawing groups. Some examples are collected in Table 4, *e.g.* the hydrolysis and solvolysis reactions of esters of carboxylic acids ([55–57]; Nos. 1–3) and sulfonic acids ([43, 58]; Nos. 4, 5) and the thermal decomposition of an urethane ([59]; No. 6).

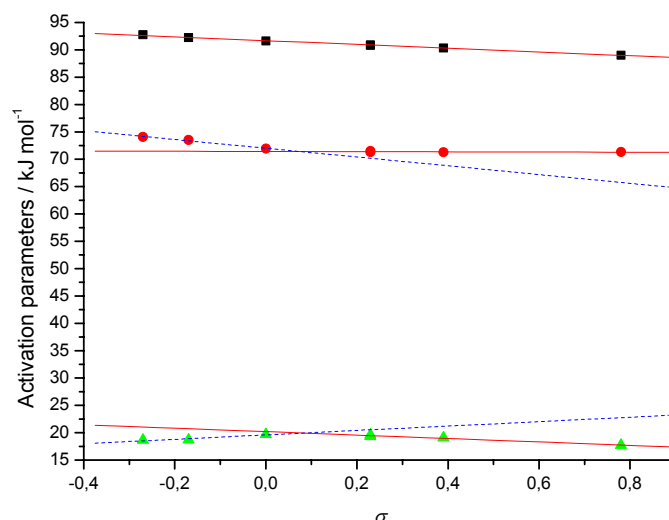


Figure 4. ΔG^\ddagger vs. σ (■—■), ΔH^\ddagger vs. σ (●—●), and $-T\Delta S^\ddagger$ vs. σ (▲—▲) plots of the alkaline hydrolysis of X-C₆H₄-C₆H₄COOEt esters (X = *p*-MeO, *p*-Me, H, *p*-Cl, *p*-Br, *m*-Br, *p*-NO₂) in 88.7 wt % ethanol–water, [55]. Reaction constants are given in Table 4. No. 1. ($T = 298$ K).

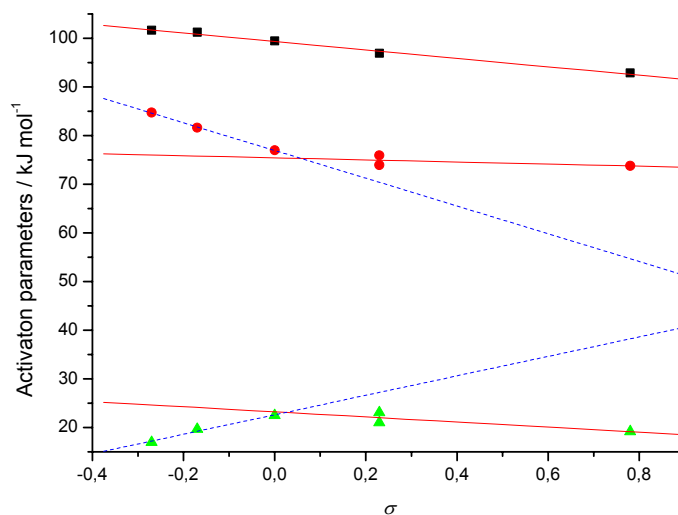


Figure 5. ΔG^\ddagger vs. σ (■—■), ΔH^\ddagger vs. σ (●—●), and $-T\Delta S^\ddagger$ vs. σ (▲—▲) plots of the alkaline hydrolysis of XC₆H₄SO₃Et esters (X = *p*-MeO, *p*-Me, H, *p*-Cl, *p*-Br, *p*-NO₂) in 70 vol % dioxane–water, [58]. Reaction constants are given in Table 4. No. 4. ($T = 323$ K).

The $\delta\Delta G^\ddagger$ reaction constants are only slightly different for compounds having the two types of substituents (Table 4. Nos. 1–5), and in many cases they have the same value within the experimental errors. Much greater and systematic changes can be observed for $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$. Both electron–withdrawing and electron–donating substituents increase the value of ΔH^\ddagger and ΔS^\ddagger , or decrease them in a smaller extent than it would be expected on the basis of a linear ΔH^\ddagger and ΔS^\ddagger vs. σ plot (e.g. Table 4, No. 2, 40 vol % dioxane–water). $\delta\Delta S^\ddagger$ and $\delta\Delta H^\ddagger$ have regularly smaller value for electron–donating substituents ($\sigma < 0$) and higher for electron–withdrawing substituents ($\sigma > 0$).

Table 4. Reaction constants of reactions with changing solvation

No	Reaction ^a	Ref.	Solvent ^b	N ^c	T/ K ^d	$\sigma \leq 0$			$\sigma \geq 0$		
						$\delta\Delta G^\ddagger$ ^e	$\delta\Delta H^\ddagger$ ^e	$\delta\Delta S^\ddagger$ ^f	$\delta\Delta G^\ddagger$ ^e	$\delta\Delta H^\ddagger$ ^e	$\delta\Delta S^\ddagger$ ^f
						(r)	(r)	(r)	(r)	(r)	(r)
1.	4-Ar-C ₆ H ₄ COOEt + OH ⁻	[55]	88.7 wt % e-w	6	298	-3.95 (0.993)	-8.03 (0.994)	-13.6 (0.941)	-3.32 (1.000)	-0.17 (0.987)	10.5
2.	ArCOOEt + OH ⁻	[56]	40 vol % d-w	5	298	-11.9 (0.999)	-12.3 (0.995)	-1.34 (0.994)	-12.5 (0.994)	-5.38 (0.995)	24.0 (0.989)
3.	ArCOSQ + OH ⁻ ^g Q = 2,4-(NO ₂) ₂ C ₆ H ₃	[57]	50 vol % d-w	9	293	-11.0 (0.981)	-25.2 (0.689)	-48.1 (0.482)	-11.2 (0.984)	22.9 (0.845)	117 (0.912)
4.	ArSO ₃ Et + OH ⁻	[58]	70 vol % d-w	6	323	-8.51 (0.981)	-28.5 (0.999)	-61.9 (0.991)	-7.37 (1.000)	-2.14 (0.555)	16.2 (0.851)
5.	ArSO ₃ CH ₂ CH=CH ₂ + EtOH	[43]	e	8	303	-10.3 (0.998)	-14.1 (0.992)	-12.6 (0.848)	-8.61 (0.995)	1.61 (0.438)	33.7 (0.965)
6.	ArNHCOOCH ₂ Ph (decomposition) ^h	[59]	eta	9	423	-8.72 (0.974)	-48.4 (0.976)	-92.9 (0.971)	-2.62 (0.864)	-5.67 (0.870)	-6.90 (0.768)

^a The σ constants were used in correlations

^b Solvent: (d) dioxane, (e) ethanol, (eta) ethanolamine (w) water. Values of solvent composition refer to the first solvent

^c Number of compounds.

^d The values of $\delta\Delta G^\ddagger$ were calculated at the given temperatures.

^e In kJ mol⁻¹ σ^{-1} unit. Values given without correlation coefficient are calculated from Eq. (5).

^f In J mol⁻¹ K⁻¹ σ^{-1} unit. Values given without correlation coefficient are calculated from Eq. (5).

^g Products: ArCOO⁻ + 2,4-(NO₂)₂C₆H₃SH

^h Products: ArN=C=O + PhCH₂OH

In connection with the Hammett equation it is well known that if the log (*k*) vs. σ plot is concave upwards the mechanism is changed with the substituents, and if the given plot is concave downward, then the rate-determining step of the reaction becomes different [4,5,60]. For the ΔG^\ddagger vs. σ plots the opposite arrangement is expected, because the sign of ρ and $\delta\Delta G^\ddagger$ are different, Eq. (8). In the decomposition of ArNHCOOCH₂Ph (Fig. 6, Table 4, No. 6) the rate-determining step of the reaction and probably also the solvation change with the substituent, because the ΔG^\ddagger vs. σ plot is concave upwards and the ΔH^\ddagger and ΔS^\ddagger vs. σ plots show breaks at $\sigma \approx 0$.

If ΔG^\ddagger gives a linear correlation with the σ constants ($\delta\Delta G^\ddagger$ is constant within the experimental errors), but $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ change with them, solvation may become different, due to the electronic effects of the substituents. $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ change together with the solvation because of the external contribution of enthalpy of activation, cf. Eq. (10). One may suppose that electron-donating groups increase the polarity of the reactant state and so diminish the difference between the reactant and the transition state, by decreasing the difference of solvation and increasing the entropy of activation (case 1 in Section 3.1). Electron-withdrawing substituent decrease the negative charge of the reactant and transition states and so the difference of the solvation of the two states, by increasing in this way the value of ΔS^\ddagger (case 2 in Section 3.1).

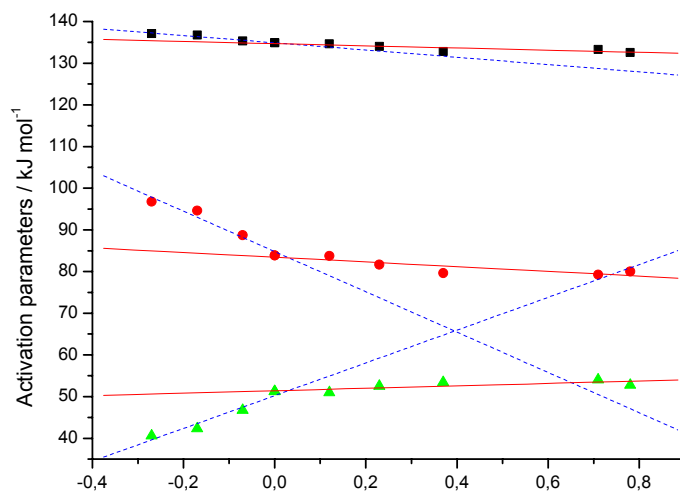


Figure 6. ΔG^\ddagger vs. σ (■—■), ΔH^\ddagger vs. σ (●—●), and $-T\Delta S^\ddagger$ vs. σ (▲—▲) plots of the decomposition of X-C₆H₄-NHCOOCH₂Ph urethanes (X = *p*-MeO, *p*-Me, *m*-Me, H, *m*-MeO, *p*-Cl, *m*-Cl, *m*-NO₂, *p*-NO₂) in ethanolamine, [59]. Reaction constants are given in Table 4. No. 6. ($T = 423$ K).

The above explanation suggests that the break of the given ΔH^\ddagger and ΔS^\ddagger vs. σ plots are not caused by a change in the mechanism or in the rate-determining step of the reaction, but by a change in the solvation. This is regularly not reflected or cause only slight differences in the free energy of activation because of the enthalpy-entropy compensation of the external parts of these activation parameters.

4 CONCLUSIONS

The ΔG^\ddagger , ΔH^\ddagger and ΔS^\ddagger activation parameters (or at least two of them) give good linear correlations with the substituent constants. The $\delta\Delta G^\ddagger$, $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ reaction constants derived from activation parameters can be used for the characterization of the effects of substituents on the reactivity and solvation in energy units. $\delta\Delta G^\ddagger \approx \delta\Delta H_{\text{int}}^\ddagger$ is a good approximation of the effect of substituents on bond formation in the reaction. $\delta\Delta S^\ddagger \approx \delta\Delta S_{\text{ext}}^\ddagger$ characterizes the change of solvation by the functional groups bonded to the reactants. $\delta\Delta H^\ddagger$ is less informative for the reaction because it has components from both the bond formation and the solvation.

$\delta\Delta G^\ddagger$ can be interpreted in the same way as the ρ constant in the Hammett equation. From the $\delta\Delta S^\ddagger$ reaction constant conclusions can be drawn on the change in solvation during the reaction, depending on the substituents in the reactants. Broken $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$ vs. σ plots refer to a change in solvation with the electronic effect of the substituents. A tentative explanation, based on the solvation of charged species and the reorganization of the solvent, is also offered for the evaluation

of the $\delta\Delta S^\ddagger$ reaction constant. The known solvation parameters [20] describe the change of reactivity for a reaction in different solvents. With the use of the $\delta\Delta S^\ddagger$ reaction constant one can characterize the change of solvation with the substituents in one solvent, that is solvation effects can be studied in a single solvent.

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Biographies

Ferenc Ruff is professor of chemistry at the Eötvös University, Budapest, Hungary. After obtaining a Ph. D. degree in 1965, Dr. Ruff joined the research group of Prof. Á. Kucsman and worked in the field of organic sulfur chemistry and physical organic chemistry. He obtained D.Sc. degree from Hungarian Academy of Sciences in 1991 and became full professor in 1992. Dr. Ruff published 95 papers and two books.

Supplementary material

Tables 5–8 present detailed statistical data (standard errors, F–statistic, standard deviation of the fit, calculated ΔG_o^\ddagger , ΔH_o^\ddagger , ΔS_o^\ddagger values, leave–one out prediction, calculated by Origin 6.1 program) for the data from Tables 1–4.

Table 5. Statistical data for reactions listed in Table 1

No	N	X	$\delta\Delta X^\ddagger$	ΔX_0^\ddagger	r	F	SD	Substituents of Ar
1a.	18	G	-13.2±0.5	87.2±0.2	0.991	839	0.816	<i>p</i> -NMe ₂ , <i>p</i> -NH ₂ , <i>p</i> -Me, <i>m</i> -NH ₂ , <i>m</i> -Me, H, <i>m</i> -MeO, <i>p</i> -F, <i>p</i> -Cl, <i>p</i> -Br, <i>p</i> -I, <i>m</i> -I, <i>m</i> -Br, <i>m</i> -Cl, <i>m</i> - CN, <i>m</i> -NO ₂ , <i>p</i> -CN, <i>p</i> -NO ₂
		H	-11.2±0.5	60.7±0.2	0.984	489	0.904	
		S	4.12±1.14	-95.3±0.7	0.668	12.9	0.612	
	13	G	-13.6±0.6	87.4±0.2	0.989	511	0.661	<i>p</i> -Me, <i>m</i> -NH ₂ , <i>m</i> -Me, H, <i>p</i> -Cl, <i>p</i> -Br, <i>p</i> -I, <i>m</i> -I, <i>m</i> -Br, <i>m</i> -Cl, <i>m</i> - NO ₂ , <i>p</i> -CN, <i>p</i> -NO ₂
		H	-11.5±0.6	60.9±0.2	0.988	438	0.608	
		S	6.54±1.31	-96.3±0.7	0.832	24.7	0.432	
1b.	5	G	-12.3±0.6	87.2±0.1	0.996	362	0.288	<i>p</i> -Me, <i>m</i> -Me, H, <i>p</i> -Cl, <i>m</i> -Cl
		H	-7.98±1.58	55.4±0.3	0.946	25.5	0.703	
		S	14.5±3.7	-107.0±0.7	0.914	15.3	0.491	
	4	G	-11.9±0.5	87.3±0.1	0.998	650	0.191	<i>p</i> -Me, <i>m</i> -Me, H, <i>m</i> -Cl
		H	-6.84±0.6	55.6±0.1	0.994	153	0.225	
		S	17.0±2.2	-106.7±0.3	0.984	60.6	0.265	
1c.	6	G	-12.7±0.4	86.6±0.1	0.998	1015	0.312	<i>p</i> -Me, <i>m</i> -Me, H, <i>p</i> -Cl, <i>m</i> -Cl, <i>p</i> - NO ₂
		H	-6.58±0.84	53.1±0.3	0.969	60.7	0.662	
		S	20.3±2.5	-122.2±1.0	0.970	63.3	0.596	
	4	G	-12.9±0.2	86.5±0.1	1.000	3121	0.155	<i>m</i> -Me, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		H	-6.08±0.5	52.7±0.2	0.993	141	0.342	
		S	22.8±1.5	-113.8±0.7	0.995	220	0.306	
1d.	6	G	-12.5±0.4	91.6±0.1	0.998	1144	0.312	<i>p</i> -Me, H, <i>m</i> -Cl, <i>m</i> -Br, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-6.19±0.70	72.5±0.3	0.975	78.1	0.590	
		S	21.2±2.2	-64.1±1.0	0.979	90.1	0.561	
	5	G	-12.8±0.5	91.8±0.3	0.998	628	0.320	H, <i>m</i> -Cl, <i>m</i> -Br, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-5.53±0.93	72.1±0.5	0.960	35.0	0.583	
		S	24.5±2.1	-65.8±1.0	0.989	134	0.392	
1e.	8	G	-14.7±0.4	91.2±0.2	0.997	1151	0.489	<i>p</i> -NH ₂ , <i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -I, <i>p</i> -Br, <i>p</i> -NO ₂
		H	-15.8±0.4	71.0±0.2	0.998	1275	0.500	
		S	-3.86±1.68	-68.1±0.7	0.685	5.3	0.563	
	5	G	-14.5±0.3	91.2±0.1	0.999	2862	0.290	<i>p</i> -NH ₂ , <i>p</i> -Me, <i>p</i> -Cl, <i>p</i> -Br, <i>p</i> - NO ₂
		H	-15.7±0.5	70.9±0.2	0.999	1028	0.524	
		S	-4.13±2.32	-68.1±0.7	0.715	3.14	0.743	
1f.	6	G	-14.5±0.6	91.1±0.3	0.996	501	0.537	<i>m</i> -Me, H, <i>p</i> -F, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-14.4±1.0	71.3±0.5	0.991	212	0.821	
		S	0.2±3.6	-66.8±1.7	0.028	0.00315	0.892	
	4	G	-15.6±0.2	91.3±0.1	1.000	7137	0.137	<i>m</i> -Me, H, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-14.7±1.1	71.7±0.6	0.995	181	0.859	
		S	0.3±3.3	-65.4±1.7	0.074	0.0109	0.759	
2.	5	G	-8.44±0.10	74.0±0.1	1.000	6814	0.0935	<i>p</i> -Me, <i>m</i> -Me, H, <i>m</i> -NO ₂ , <i>p</i> - NO ₂
		H	-8.53±0.23	51.1±0.1	0.999	1368	0.206	
		S	0.1±0.8	-79.5±0.3	0.0857	0.0222	0.232	
	4	G	-8.39±0.11	73.9±0.1	1.000	5679	0.0927	<i>p</i> -Me, H, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-8.23±0.23	51.0±0.1	0.999	1292	0.191	
		S	0.3±1.1	-79.6±0.7	0.203	0.086	0.272	
3a.	7	G	-6.07±0.33	75.2±0.1	0.993	345	0.308	<i>m</i> -NH ₂ , <i>m</i> -Me, H, <i>p</i> -F, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-5.19±0.47	42.4±0.2	0.981	124	0.439	
		S	3.20±1.51	-110.1±0.7	0.684	4.39	0.429	
	5	G	-6.40±0.35	75.4±0.2	0.996	331	0.245	H, <i>p</i> -F, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-4.81±0.45	42.2±0.2	0.987	114	0.314	
		S	5.10±2.0	-111.4±1.0	0.821	6.23	0.425	
3b.	6	G	-9.44±0.32	69.6±0.2	0.998	876	0.263	<i>m</i> -Me, H, <i>p</i> -F, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-16.0±1.1	36.1±0.5	0.991	212	0.905	
		S	-22.4±4.4	-112.4±2.0	0.931	26.2	1.078	
	4	G	-9.64±0.26	69.7±0.2	0.999	1330	0.169	H, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-16.6±0.44	36.4±0.3	0.999	1403	0.284	
		S	-23.7±2.6	-112.4±1.3	0.988	79.8	0.503	

Table 5. (Continued)

No	N	X	$\delta\Delta X^\ddagger$	ΔX_0^\ddagger	<i>r</i>	F	SD	Substituents of Ar
3c.	6	<i>G</i>	-13.0±0.5	79.1±0.2	0.997	712	0.402	<i>m</i> -Me, H, <i>p</i> -F, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-24.9±2.8	63.6±1.3	0.976	80.5	2.284	
		<i>S</i>	-39.6±8.1	-52.3±4.0	0.924	23.2	2.020	
	4	<i>G</i>	-13.2±0.4	79.1±0.2	0.999	1053	0.283	H, <i>p</i> -F, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-26.1±1.6	63.7±0.1	0.996	269	1.108	
		<i>S</i>	-43.3±6.4	-52.0±3.4	0.979	46.7	1.310	
4.	4	<i>G</i>	-8.49±0.18	111.9±0.1	1.000	2243	0.128	<i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		<i>H</i>	-12.6±1.2	74.4±0.5	0.991	103	0.883	
		<i>S</i>	-12.9±4.3	-115.0±2.0	0.901	8.63	1.026	
	3	<i>G</i>	-8.40±0.28	111.8±0.1	0.999	892	0.159	H, <i>p</i> -Cl, <i>p</i> -NO ₂
		<i>H</i>	-12.9±2.1	74.6±1.0	0.987	36.8	1.206	
		<i>S</i>	-14.1±7.6	-114.0±3.7	0.881	3.46	1.403	
5.	9	<i>G</i>	-19.8±0.8	102.6±0.3	0.994	605	0.877	<i>p</i> -MeO, <i>p</i> -Me, <i>p</i> -tBu, <i>m</i> -Me, H, <i>m</i> -MeO, <i>p</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> - NO ₂
		<i>H</i>	-31.3±2.9	67.1±1.1	0.971	115	3.180	
		<i>S</i>	-38.6±9.1	-156.7±3.1	0.852	18.5	2.901	
	5	<i>G</i>	-20.2±1.2	102.9±0.6	0.995	308	1.022	<i>p</i> -Me, <i>m</i> -Me, <i>m</i> -MeO, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-30.9±2.2	67.0±1.0	0.993	203	1.922	
		<i>S</i>	-35.9±8.1	-158.1±4.0	0.933	20.1	2.118	
6.	4	<i>G</i>	-11.2±0.1	97.3±0.1	1.000	9469	0.083	<i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		<i>H</i>	-23.0±1.1	48.1±0.5	0.998	431	0.792	
		<i>S</i>	-39.3±3.4	-165.0±1.0	0.993	139	0.713	
	3	<i>G</i>	-11.2±0.2	97.3±0.1	1.000	5305	0.111	<i>p</i> -Me, H, <i>p</i> -NO ₂
		<i>H</i>	-23.0±1.6	48.1±0.7	0.998	216	1.118	
		<i>S</i>	-39.3±4.7	-165.0±2.0	0.993	69.4	1.017	
7a.	6	<i>G</i>	-8.83±0.69	90.9±0.3	0.988	165	0.559	H, <i>p</i> -F, <i>p</i> -I, <i>p</i> -Cl, <i>p</i> -Br, <i>p</i> -NO ₂
		<i>H</i>	-15.4±1.2	61.8±0.5	0.989	175	0.944	
		<i>S</i>	-21.9±3.7	-98.0±1.5	0.948	35.2	0.985	
	5	<i>G</i>	-8.85±0.78	90.9±0.4	0.989	128	0.632	H, <i>p</i> -F, <i>p</i> -Cl, <i>p</i> -Br, <i>p</i> -NO ₂
		<i>H</i>	-15.2±1.1	61.9±0.5	0.993	199	0.874	
		<i>S</i>	-21.4±2.8	-97.0±1.3	0.975	58.0	0.680	
7b.	6	<i>G</i>	-10.4±0.7	96.7±0.4	0.989	186	0.617	<i>m</i> -Me, H, <i>m</i> -MeO, <i>m</i> -Br, <i>m</i> - NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-16.6±1.3	57.1±0.6	0.988	166	1.044	
		<i>S</i>	-20.9±3.5	-133.0±2.0	0.948	35.4	0.852	
	5	<i>G</i>	-9.97±0.4	96.3±0.2	0.998	607	0.317	<i>m</i> -Me, H, <i>m</i> -Br, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-16.1±1.1	56.7±0.6	0.993	203	0.883	
		<i>S</i>	-20.5±4.0	-133.0±2.0	0.944	24.6	0.966	
8	4	<i>G</i>	-6.85±0.56	79.5±0.2	0.993	148	0.404	<i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		<i>H</i>	-9.34±0.74	28.9±0.3	0.994	158	0.533	
		<i>S</i>	-9.02±1.84	-170.0±1.0	0.960	23.6	0.398	
	3	<i>G</i>	-6.88±0.47	79.7±0.2	0.998	212	0.337	<i>p</i> -Me, H, <i>p</i> -NO ₂
		<i>H</i>	-9.37±0.30	28.8±0.1	0.999	949	0.218	
		<i>S</i>	-9.09±2.15	-171.0±1.0	0.973	17.8	0.459	
9a.	5	<i>G</i>	14.2±1.1	80.7±0.7	0.992	178	1.066	H, <i>p</i> -Cl, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	14.0±1.9	30.3±1.3	0.975	56.9	1.850	
		<i>S</i>	-0.9±6.3	-169.0±4.0	0.081	0.0202	1.865	
	4	<i>G</i>	13.9±0.7	80.5±0.4	0.998	424	0.655	H, <i>p</i> -Cl, <i>m</i> -Cl, <i>p</i> -NO ₂
		<i>H</i>	13.6±1.1	30.1±1.3	0.980	47.9	1.909	
		<i>S</i>	-1.0±7.8	-169.0±5.4	0.080	0.0159	2.283	
9b	4	<i>G</i>	14.8±1.2	78.2±0.9	0.993	146	1.212	H, <i>p</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	19.3±0.6	22.9±0.4	0.999	1118	0.571	
		<i>S</i>	12.5±4.7	-185.0±3.4	0.884	7.15	1.374	
	3	<i>G</i>	14.5±0.7	78.0±0.5	0.999	439	0.672	H, <i>p</i> -Cl, <i>p</i> -NO ₂
		<i>H</i>	19.5±0.2	23.0±0.1	1.000	10600	0.183	
		<i>S</i>	13.8±1.2	-184.2±1.0	0.996	127	0.353	

Table 6. Statistical data for reactions listed in Table 2

No	N	X	$\delta\Delta X^\ddagger$	ΔX_0^\ddagger	r	F	SD	Substituents of Ar
1.	6	G	-5.72±0.66	102.1±0.3	0.974	74.5	0.661	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Br, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-1.53±0.56	86.7±0.3	0.808	7.53	0.556	
		S	12.9±1.5	-48.3±0.6	0.973	72.0	0.491	
	4	G	-5.85±1.09	102.0±0.5	0.967	28.9	0.897	<i>p</i> -MeO, <i>p</i> -Me, <i>p</i> -Br, <i>p</i> -NO ₂
		H	-2.15±0.41	86.8±0.2	0.964	26.7	0.344	
		S	11.3±1.1	-48.0±0.6	0.991	105	0.294	
2.	5	G	-9.29±0.19	111.6±0.1	0.999	2323	0.150	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Br, <i>m</i> -NO ₂
		H	-2.16±1.23	87.8±0.4	0.711	3.07	0.963	
		S	22.8±4.5	-76.0±1.6	0.946	25.5	1.101	
	4	G	9.37±0.20	111.6±0.1	1.000	2138	0.145	<i>p</i> -MeO, H, <i>p</i> -Br, <i>m</i> -NO ₂
		H	-1.38±0.79	87.4±0.3	0.777	3.05	0.567	
		S	25.6±3.2	-77.3±1.3	0.985	64.9	0.714	
3a.	6	G	-7.75±0.59	111.6±0.3	0.989	175	0.585	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-2.35±0.55	89.0±0.3	0.904	18.0	0.553	
		S	17.2±2.0	-72.2±1.0	0.975	76.5	0.615	
	4	G	-7.01±0.62	111.6±0.3	0.992	128	0.480	<i>p</i> -MeO, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		H	-1.88±0.43	89.2±0.2	0.952	19.1	0.333	
		S	16.4±3.1	-71.6±1.3	0.966	28.1	0.748	
3b.	6	G	-8.05±0.71	113.0±0.3	0.985	127	0.712	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-0.51±0.70	87.1±0.3	0.344	0.536	0.694	
		S	24.2±3.4	-82.7±1.6	0.963	50.8	1.058	
	4	G	-7.14±0.76	112.9±0.3	0.989	89.0	0.585	<i>p</i> -MeO, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		H	-0.17±0.37	86.7±0.2	0.314	0.219	0.287	
		S	22.2±3.6	-83.7±1.6	0.975	39.0	0.858	
3c.	6	G	-8.33±0.70	113.4±0.3	0.986	144	0.693	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	0.34±0.79	83.5±0.4	0.210	0.185	0.787	
		S	27.7±3.0	-95.2±1.3	0.977	85.5	0.934	
	4	G	-7.51±0.76	113.5±0.3	0.990	96.8	0.590	<i>p</i> -MeO, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		H	0.23±0.94	83.9±0.4	0.168	0.0577	0.724	
		S	24.6±3.7	-94.2±1.6	0.978	44.6	0.893	
3d.	6	G	-8.39±0.67	113.7±0.3	0.988	157	0.666	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-1.77±0.93	86.3±0.4	0.691	3.65	0.926	
		S	21.1±4.3	-87.5±1.9	0.955	23.6	1.354	
	4	G	-7.68±0.82	113.8±0.3	0.989	87.9	0.587	<i>p</i> -MeO, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		H	-1.47±0.23	85.7±0.1	0.976	39.9	0.168	
		S	19.7±2.4	-89.5±1.0	0.985	65.8	0.545	
3e.	6	G	-9.16±0.74	114.4±0.3	0.987	152	0.740	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-1.00±0.63	74.9±0.3	0.624	2.55	0.626	
		S	26.1±3.9	-126.2±1.9	0.957	43.9	1.229	
	4	G	-8.28±0.84	114.4±0.4	0.990	96.5	0.651	<i>p</i> -MeO, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		H	-1.93±0.15	75.2±0.1	0.994	171	0.114	
		S	20.3±3.1	-125.2±1.3	0.978	43.4	0.744	
3f.	6	G	-9.77±0.71	118.1±0.3	0.990	189	0.708	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-0.64±0.36	75.8±0.2	0.661	3.10	0.360	
		S	29.2±2.0	-135.1±1.0	0.990	200	0.664	
	4	G	-8.92±0.79	118.1±0.3	0.992	126	0.613	<i>p</i> -MeO, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		H	-0.76±0.31	76.0±0.1	0.848	5.10	0.240	
		S	26.2±1.7	-134.5±0.6	0.996	239	0.410	
4a.	8	G	-8.39±0.14	100.6±0.1	0.999	3350	0.146	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -Br, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-7.53±1.23	86.9±0.5	0.929	37.5	1.238	
		S	2.87±3.96	-45.5±1.7	0.284	0.526	1.207	
	5	G	-8.39±0.17	100.6±0.1	0.999	2572	0.165	<i>p</i> -MeO, <i>p</i> -Me, H, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-7.60±0.95	87.3±0.5	0.977	64.1	0.946	
		S	2.67±3.47	-43.9±1.7	0.405	0.589	1.048	

Table 6. (Continued)

No	N	X	$\delta\Delta X^\ddagger$	ΔX_0^\ddagger	<i>r</i>	F	SD	Substituents of Ar
4b.	8	<i>G</i>	-8.95±0.20	103.3±0.1	0.998	1800	0.213	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -Br, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-4.77±1.50	88.4±0.6	0.796	10.2	1.513	
		<i>S</i>	13.8±4.5	-48.8±2.0	0.783	9.46	1.371	
	5	<i>G</i>	-9.00±0.19	103.3±0.1	0.999	2163	0.193	<i>p</i> -MeO, <i>p</i> -Me, H, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-5.08±1.59	88.5±0.8	0.880	10.3	1,580	
		<i>S</i>	13.0±5.0	-48.8±2.3	0.832	6.73	1,510	
4c.	8	<i>G</i>	-9.22±0.22	103.5±0.1	0.998	1751	0.223	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -Br, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-2.47±0.58	87.4±0.2	0.868	18.1	0.587	
		<i>S</i>	22.3±2.3	-53.5±1.0	0.970	95.0	0.701	
	5	<i>G</i>	-9.26±0.22	103.6±0.1	0.999	1829	0.216	<i>p</i> -MeO, <i>p</i> -Me, H, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-2.39±0.30	87.2±0.1	0.977	62.9	0.301	
		<i>S</i>	22.7±0.6	-54.1±0.3	0.999	1472	0.179	
4d.	8	<i>G</i>	-9.36±0.23	104.7±0.1	0.998	1725	0.228	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -Br, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-1.08±0.89	82.3±0.4	0.442	1.460	0.901	
		<i>S</i>	27.4±3.2	-73.9±1.3	0.962	73.5	0.979	
	5	<i>G</i>	-9.40±0.23	104.7±0.1	0.999	1717	0.226	<i>p</i> -MeO, <i>p</i> -Me, H, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-1.12±1.24	82.3±0.6	0.464	0.822	1.240	
		<i>S</i>	27.4±4.6	-74.3±2.3	0.961	36.4	1.372	
4e.	8	<i>G</i>	-10.4±0.3	106.0±0.1	0.998	1559	0.267	<i>p</i> -MeO, <i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -Br, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-2.93±0.87	60.1±0.4	0.808	11.3	0.883	
		<i>S</i>	24.8±2.8	-125.0±1.3	0.964	78.0	0.859	
	5	<i>G</i>	-10.5±0.2	106.0±0.1	0.999	2080	0.229	<i>p</i> -MeO, <i>p</i> -Me, H, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-3.18±0.42	67.6±0.2	0.975	56.9	0.420	
		<i>S</i>	24.2±0.9	-127.0±0.1	0.998	759	0.265	
5.	7	<i>G</i>	13.8±0.7	100.9±0.1	0.994	398	0.273	<i>p</i> -MeO, <i>p</i> -Me, <i>m</i> -Me, H, <i>p</i> -F, <i>p</i> -Cl, <i>p</i> -Ph
		<i>H</i>	16.7±1.8	61.1±0.3	0.974	90.7	0.691	
		<i>S</i>	8.99±5.3	-121.3±0.9	0.604	2.87	0.685	
	5	<i>G</i>	13.9±0.8	100.9±0.1	0.995	330	0.298	<i>p</i> -MeO, <i>p</i> -Me, <i>p</i> -F, <i>p</i> -Cl, <i>p</i> -Ph
		<i>H</i>	16.5±1.9	61.1±0.3	0.980	73.5	0.750	
		<i>S</i>	7.99±4.88	-121.0±0.9	0.688	2.70	0.623	
6	10	<i>G</i>	-0.70±0.05	142.5±0.1	0.977	165	0.0624	<i>p</i> -MeO, 3,4-Me ₂ , <i>p</i> -Me, <i>m</i> -Me, H, <i>p</i> -Br, <i>p</i> -I, <i>p</i> -MeCO, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-36.1±1.5	81.7±0.6	0.993	530	1.801	
		<i>S</i>	-77.2±3.5	-131.5±1.3	0.992	522	1.788	
	7	<i>G</i>	-0.70±0.06	142.5±0.1	0.984	157	0.0601	<i>p</i> -MeO, 3,4-Me ₂ , <i>m</i> -Me, H, <i>p</i> -MeCO, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		<i>H</i>	-36.6±0.8	82.2±0.4	0.999	2013	0.888	
		<i>S</i>	-78.1±1.7	-130.4±0.9	0.999	1867	0.909	
7.	14	<i>G</i>	13.8±0.6	89.7±0.3	0.988	500	0.808	<i>p</i> -Me, <i>m</i> -Me, H, <i>p</i> -F, <i>p</i> -Cl, <i>p</i> -Br, <i>p</i> -I, <i>m</i> -Br, <i>p</i> -COOH, <i>p</i> -COOMe, <i>m</i> -CN, <i>m</i> -NO ₂ , <i>p</i> -SO ₂ NH ₂ , <i>p</i> -CN
		<i>H</i>	26.1±1.1	74.3±0.6	0.989	535	1.48	
		<i>S</i>	41.3±2.3	-51.7±1.0	0.982	328	0.894	
	8	<i>G</i>	14.6±0.7	89.5±0.3	0.993	402	0.619	<i>p</i> -Me, <i>m</i> -Me, <i>p</i> -Cl, <i>m</i> -Br, <i>p</i> -COOH, <i>p</i> -COOMe, <i>m</i> -CN, <i>m</i> -NO ₂
		<i>H</i>	27.4±0.7	73.7±0.3	0.998	1494	0.603	
		<i>S</i>	43.0±2.0	-53.0±1.0	0.993	449	0.515	

Table 7. Statistical data for reactions listed in Table 3

No	N	X	$\delta\Delta X^\ddagger$	ΔX_0^\ddagger	r	F	SD	Substituents of Ar
1a.	8	G	-1.83±0.45	119.4±0.2	0.855	16.3	0.516	<i>p</i> -MeO, <i>p</i> -OH, <i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -Br, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-9.21±1.65	78.8±0.7	0.916	31.2	1.876	
		S	-20.5±4.3	-115.0±1.7	0.890	23.0	1,718	
	6	G	-2.29±0.57	119.4±0.2	0.896	16.2	0.509	<i>p</i> -OH, <i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -Br, <i>p</i> -NO ₂
		H	-10.4±0.6	78.0±0.2	0.994	345	0.500	
		S	-22.8±2.8	-117.0±1.1	0.971	65.5	0.889	
	5	G	-1.54±0.38	119.1±0.1	0.920	16.5	0.271	<i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -Br, <i>p</i> -NO ₂
		H	-10.7±0.8	78.1±0.3	0.992	196	0.546	
		S	-26.0±2.6	-115.9±1.1	0.985	97.1	0.668	
1b.	8	G	-1.68±0.50	119.5±0.2	0.808	11.3	0.568	<i>p</i> -MeO, <i>p</i> -OH, <i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -Br, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-3.34±0.83	82.5±0.4	0.854	16.1	0.945	
		S	-4.79±1.87	-104.8±0.8	0.724	6.61	0.749	
	6	G	-0.86±0.49	119.1±0.2	0.669	3.24	0.406	<i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -Br, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-2.13±0.72	81.9±0.3	0.829	8.82	0.609	
		S	-3.91±1.53	-105.3±0.6	0.790	6.62	0,456	
	5	G	-1.30±0.45	119.1±0.2	0.856	8.21	0.325	<i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -Br, <i>p</i> -NO ₂
		H	-2.68±0.78	81.9±0.3	0.894	12.0	0.556	
		S	-4.56±1.95	-105.4±0.8	0.803	5,43	0.496	
2.	5	G	0.94±0.12	99.2±0.1	0.976	59.6	0.0942	<i>p</i> -Me, <i>m</i> -Me, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		H	-2.01±0.37	69.2±0.1	0.951	28.7	0.291	
		S	-9.80±1.0	-100.7±0.3	0.985	96.1	0.231	
	4	G	0.96±0.13	99.2±0.1	0.980	48.1	0.103	<i>p</i> -Me, <i>m</i> -Me, H, <i>p</i> -NO ₂
		H	-2.09±0.17	69.2±0.1	0.993	146	0.133	
		S	-10.0±0.3	-100.7±0.1	0.999	1550	0.0584	
3.	4	G	2.69±0.16	115.0±0.1	0.997	284	0.114	<i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		H	11.3±3.0	92.3±1.2	0.957	14.4	2.130	
		S	26.3±10.4	-69.9±4.4	0.891	7.68	2.218	
	3	G	2.80±0.22	115.0±0.1	0.997	167	0.123	H, <i>p</i> -Cl, <i>p</i> -NO ₂
		H	8.06±3.09	94.0±0.4	0.994	88.7	0.485	
		S	17.6±3.6	-70.5±2.0	0.980	24.0	0.608	
4a.	6	G	-0.81±0.02	77.1±0.1	0.999	1520	0.0197	<i>p</i> -MeO, <i>p</i> -OH, <i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		H	-40.4±2.1	63.2±0.8	0.995	370	1.986	
		S	-132.8±7.0	-46.6±2.7	0.994	356	1.984	
	4	G	-0.81±0.02	77.1±0.1	0.999	1166	0.0217	<i>p</i> -MeO, <i>p</i> -OH, <i>p</i> -Me, <i>p</i> -NO ₂
		H	-40.1±0.5	62.7±0.2	1.000	5632	0.492	
		S	-131.9±1.7	-48.3±0.7	1.000	5767	0.476	
4b.	6	G	0.94±0.07	89.1±0.1	0.989	184	0.066	<i>p</i> -MeO, <i>p</i> -OH, <i>p</i> -Me, H, <i>p</i> -Cl, <i>p</i> -NO ₂
		H	-36.7±1.2	36.6±0.5	0.998	866	1.178	
		S	-125.8±4.0	-176.2±1.7	0.998	927	1.163	
	5	G	0.95±0.08	89.2±0.1	0.990	144	0.073	<i>p</i> -MeO, <i>p</i> -OH, <i>p</i> -Me, H, <i>p</i> -NO ₂
		H	-36.3±1.1	36.9±0.5	0.999	1028	1.042	
		S	-124.5±3.7	-175.2±1.3	0.999	1168	0.999	
5.	16	G	1.33±0.67	95.0±0.2	0.464	3.83	0.802	<i>p</i> -MeO, <i>p</i> -EtO, <i>p</i> -Me, <i>m</i> -Me, H, <i>m</i> -MeO, <i>m</i> -EtO, <i>p</i> -F, <i>m</i> -F, <i>p</i> -Cl, <i>m</i> -Cl, <i>p</i> -Br, <i>m</i> -Br, <i>m</i> -I, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	1.10±1.25	57.4±0.4	0.228	0.770	1.484	
		S	-0.7±5.2	-126.0±2.0	0.0357	0.0178	1.823	
	11	G	1.13±0.69	95.0±0.3	0.482	2.735	0.745	<i>p</i> -MeO, <i>p</i> -EtO, <i>m</i> -EtO, <i>p</i> -F, <i>m</i> -F, <i>m</i> -Cl, <i>p</i> -Br, <i>m</i> -Br, <i>m</i> -I, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	1.22±0.37	57.1±0.2	0.738	10.8	0.403	
		S	0.4±2.2	-128.0±1.0	0.057	0.0292	0.724	
6.	14	G	-3.46±0.54	111.0±0.1	0.871	41.1	0.548	<i>p</i> -MeO, <i>p</i> -EtO, <i>p</i> -Me, <i>m</i> -Me, H, <i>m</i> -MeO, <i>m</i> -EtO, <i>p</i> -F, <i>m</i> -F, <i>p</i> -Cl, <i>m</i> -Cl, <i>m</i> -Br, <i>m</i> -I, <i>m</i> -NO ₂
		H	-5.96±3.71	76.1±1.1	0.407	2.59	3.76	
		S	-7.83±11.1	-105.8±3.2	0.192	0.500	3.70	
	9	G	-2.18±0.27	110.6±0.1	0.942	63.3	0.208	<i>p</i> -Me, H, <i>m</i> -MeO, <i>m</i> -EtO, <i>m</i> -F, <i>p</i> -Cl, <i>m</i> -Cl, <i>m</i> -Br, <i>m</i> -NO ₂ ,
		H	-4.56±2.80	76.7±0.1	0.500	2.66	2.13	
		S	-7.74±8.57	-103.0±2.7	0.304	0–817	2.14	

Table 7. (Continued)

No	N	X	$\delta\Delta X^\ddagger$	ΔX_0^\ddagger	<i>r</i>	F	SD	Substituents of Ar
7.	8	<i>G</i>	-12.9±0.3	84.3±0.2	0.999	2479	0.400	<i>p</i> -MeO, <i>p</i> -Me, <i>m</i> -Me, <i>p</i> -tBu, H, <i>m</i> -Br, <i>m</i> -NO ₂ , 3,5-(NO ₂) ₂
		<i>H</i>	-9.03±2.9	51.9±1.8	0.778	9.2	4.54	
		<i>S</i>	13.5±9.3	-109.1±5.4	0.508	2.08	4.24	
	5	<i>G</i>	-12.9±0.2	84.5±0.2	0.999	2902	0.332	<i>p</i> -MeO, <i>m</i> -Me, <i>p</i> -tBu, H, 3,5-(NO ₂) ₂
		<i>H</i>	-11.1±0.7	53.1±0.5	0.993	224	1.01	
		<i>S</i>	6.68±3.15	-105.7±2.0	0.773	4.45	1.31	
8	8	G	9.59±0.35	83.6±0.2	0.996	735	0.577	4,4'-(MeO) ₂ , 4,4'-Me ₂ , H, 4-Cl, 4-Br, 4,4'-Cl ₂ , 3-NO ₂ , 3,3'-(NO ₂) ₂
		H	5.16±0.90	53.3±0.6	0.919	32.6	1,472	
		S	-14.9±3.1	-102.0±2.0	0.890	22.8	1.502	
	6	G	9.73±0.44	83.5±0.3	0.996	482	0.660	4,4'-(MeO) ₂ , H, 4-Cl, 4-Br, 3-NO ₂ , 3,3'-(NO ₂) ₂
		H	4.50±0.54	53.3±0.4	0.972	69.3	0.804	
		S	-17.4±0.9	-101.0±0.7	0.995	388	0.393	
9	5	G	-8.79±0.93	98.4±0.2	0.984	89.5	0.413	<i>p</i> -Me, <i>m</i> -Me, H, <i>p</i> -Cl, <i>m</i> -Cl
		H	-21.2±0.6	21.9±0.1	0.999	1438	0.249	
		S	-37.4±1.8	-232.5±0.3	0.996	373	0.283	
	4	G	-9.29±0.70	98.6±0.2	0.994	176	0.291	<i>p</i> -Me, H, <i>p</i> -Cl, <i>m</i> -Cl
		H	-21.5±0.6	22.0±0.1	0.999	1355	0.242	
		S	-36.5±1.5	-232.8±0.3	0.998	496	0.223	
10	4	G	16.2±1.0	98.2±0.2	0.997	285	0.397	<i>p</i> -Me, H, <i>p</i> -Cl, <i>m</i> -Cl
		H	20.0±0.9	21.5±0.2	0.998	510	0.368	
		S	12.1±2.5	-232.8±0.6	0.959	23.1	0.343	
	3	G	16.6±0.2	98.3±0.1	1.000	6545	0.0803	<i>p</i> -Me, H, <i>m</i> -Cl
		H	20.2±1.2	21.5±0.3	0.998	271	0.479	
		S	11.2±2.9	-233.0±0.6	0.968	15.1	0.372	

Table 8. Statistical data for reactions listed in Table 4

No	N	X	$\delta\Delta\ddagger$	ΔX_0^\ddagger	r	F	SD	Substituents of Ar
1.	3	G	-3.95±0.47	91.6±0.1	0.993	69.5	0.09	<i>p</i> -MeO, <i>p</i> -Me, H
		H	-8.03±0.97	72.0±0.2	0.994	68.3	0.187	
		S	-13.6±4.9	-65.8±1.0	0.941	7.70	0.281	
	4	G	-3.32±0.03	91.6±0.1	1.000	9590	0.0153	<i>p</i> -Cl, <i>p</i> -Br, <i>m</i> -Cl, <i>p</i> -NO ₂
		H	-0.17±0.32	71.4±0.1	0.345	0.269	0.144	
		S	10.5±1.2	-67.8±0.7	0.987	72.7	0.165	
2.	3	G	-11.9±0.5	85.6±0.2	0.999	675	0.221	<i>p</i> -NH ₂ , <i>p</i> -Me, H
		H	-12.3±1.2	51.9±0.5	0.995	101	0.590	
		S	-1.28±2.55	-113.1±1.0	0.450	0.253	0.369	
	3	G	-12.5±1.7	85.9±0.9	0.994	52.6	0.949	H, <i>m</i> -Cl, <i>p</i> -NO ₂
		H	-5.38±0.65	51.7±0.3	0.995	67.4	0.359	
		S	24.0±3.6	-114.4±1.7	0.989	44.6	0.590	
3.	4	G	-11.0±1.56	60.5±0.3	0.981	50.0	0.301	<i>p</i> -MeO, <i>m</i> -NMe ₂ , <i>p</i> -Me, H
		H	-25.2±18.7	92.0±3.3	0.689	1.81	3.62	
		S	-48.1±61.8	-107.8±11.0	0.482	0.605	3.50	
	7	G	-11.2±0.9	60.8±0.3	0.984	156	0.544	H, <i>m</i> -MeO, <i>p</i> -Cl, <i>p</i> -Br, <i>m</i> -I, <i>m</i> -Cl, <i>p</i> -NO ₂
		H	22.9±16.0	93.1±6.0	0.845	2.64	9.72	
		S	117.0±5.6	-110.6±20.8	0.912	5.25	9.94	
4.	3	G	-8.51±1.65	99.6±0.3	0.981	26.6	0.318	<i>p</i> -MeO, <i>p</i> -Me, H
		H	-28.5±1.1	76.9±0.2	0.999	736	0.203	
		S	-61.9±8.4	-70.0±1.5	0.991	55.0	0.521	
	3	G	-7.37±0.02	98.7±0.1	1.000	210000	0.00722	<i>p</i> -Cl, <i>p</i> -Br, <i>p</i> -NO ₂
		H	-2.14±3.20	75.4±1.6	0.555	0.446	1.439	
		S	16.2±1.0	-71.8±5.0	0.851	2.637	1.447	
5.	3	G	-10.3±0.6	102.4±0.1	0.998	304	0.114	<i>p</i> -MeO, <i>p</i> -Me, H
		H	-14.1±1.8	82.9±0.3	0.992	61.3	0.348	
		S	-12.6±7.9	-64.4±1.3	0.848	2.55	0.461	
	5	G	-8.61±0.51	102.5±0.3	0.995	288	0.266	<i>p</i> -Cl, <i>p</i> -Br, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	1.61±1.90	80.7±1.0	0.438	0.714	0.997	
		S	33.7±5.3	-71.9±2.6	0.965	40.3	0.845	
6.	4	G	-8.72±1.43	134.9±0.2	0.974	37.2	0.292	<i>p</i> -MeO, <i>p</i> -Me, <i>m</i> -Me, H
		H	-48.4±7.7	84.8±1.2	0.976	39.6	1.568	
		S	-92.9±16.3	-118.7±2.6	0.971	32.7	1.405	
	6	G	-2.62±0.76	134.7±0.4	0.864	11.8	0.541	H, <i>m</i> -MeO, <i>p</i> -Cl, <i>m</i> -Cl, <i>m</i> -NO ₂ , <i>p</i> -NO ₂
		H	-5.67±1.60	83.4±0.8	0.870	12.5	1.136	
		S	-6.90±2.88	-121.5±1.4	0.768	5.74	0.865	